REMARKS

Initially, at page 2 of the Office Action, Claims 1, 2, 7-10, 13 and 14 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

These claims have been amended as suggested by the Examiner to overcome these formal rejections. Specifically, Claims 1 and 2 have been corrected to reflect proper Markush form, antecedent basis have been added to Claims 13 and 14, and phrases within parentheses were removed from Claims 7 and 8. In Claims 9 and 10, E110, which is the E.C. number and equivalent to FD&C Yellow 6 has been defined by its common name, i.e., Sunset Yellow. See attached Remington's The Science and Practice of Pharmacy, 20th ed., Lippincott Williams & Wilkins, 2000, p. 949.

Turning to the substantive matters raised, at page 3 of the Office Action Claims 1, 2, 4, 5, 7, 8, 15 and 17 were rejected under 35 U.S.C. 102(b) as being anticipated by FR-A-2073271 (hereinafter FR '271).

Applicant respectfully transverses the rejection and requests reconsideration thereof.

At page 5 of the Office Action, Claims 1-8 and 15-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over FR '271.

Reconsideration is respectfully requested.

With respect to the primary reference, FR '271, a composition comprising Vitamin D_2, calcium gluconate, oil, paraffin and Tesal is disclosed. As stated by the Examiner "the reference does not disclose the amounts of vitamin D and calcium salt in the manner claimed by the applicant, and therefore, there is no means for a comparison."

The preparation of the present application is not set forth in FR '271. The present application discloses novel homogeneous pharmaceutical compositions containing Vitamin D and calcium in a specific ratio which overcome prior art disadvantages. Calcium as the phosphate, glycerophosphate, carbonate, bicarbonate, lactate, citrate, tartrate, gluconate or chloride salts may be utilized. Vitamin D as D_2, D_3 or a mixture may be utilized. The claimed composition also contains limited amounts of

propylene glycol, polyethylene glycol, liquid paraffin, silicone oil which only function as a binder.

Unlike the present invention, in FR '271, Vitamin D must be in the form of Vitamin D_2 and the calcium salt must be one which is capable of being absorbed topically, e.g. gluconate (see page 2, line 24). The FR '271 reference cannot and does not utilize calcium salts which cannot be topically absorbed, e.g. calcium carbonate. Conversely, the present application discloses water insoluble calcium salts unsuitable for dermatological creams since they cannot penetrate the dermal layer. As such, FR' 271 actually teaches away from the present invention.

The FR' 271 formulation contains Tesal, a polyethylene glycol stearate, i.e., a fat having physico-chemical properties, such as viscosity which differs greatly from the polyalcohols of the present invention. Polyethylene glycol and propylene glycol of the present application are liquids with very low viscosity. Further, the ratio of calcium to Vitamin D_2 is between 500:1 to 125:1 and the amount of elemental calcium in the cream is approximately 1.8%. The present invention is distinguished in that it contains between 11.6 and 31% of elemental calcium. The 500-1000 I.U. of Vitamin D corresponds to 12.5-25 mcg of Vitamin D_2. For the present application, the ratio of calcium to Vitamin D_2 is between 160,000:1 to 40,000:1. Thus, ratio of calcium to Vitamin D is 320 times less in FR '271 than the present application.

FR '271 describes dermatological creams for topical use (see example, p. 2). Nowhere in the disclosure of FR '271 is a liquid pharmaceutical for oral use suggested. The present application at page 4, lines 7-9 expressly states that the claimed compositions are not suitable for dermatological use.

The present invention is distinctly different from FR '271, which does not teach or address main features of the Applicant's invention. The present application is based on granulate as described in example 7 and 8 and claims 13 and 14, i.e. bags and tablets. A granulate cannot be used for dermatological use. Notwithstanding, no teaching is provided that would motivate anyone to modify FR '271.

At page 4 of the Office Action, Claims 1-7 were rejected under 35 U.S.C. 102(b) as being anticipated by EP 588 539A to Silver.

Reconsideration is requested.

The Examiner stated "the reference does not disclose the amounts of Vitamin D and calcium salt in the same manner claimed by the Applicant, and therefore, there is no means for comparison."

Silver discloses a composition of Vitamin D_2 and Vitamin D_3 derivatives, an antioxidant, and a solid pharmaceutical excipient or carrier. Silver does not disclose calcium in combination with Vitamin D. In Silver, calcium phosphate may be used as an excipient but lactose or sorbitol may alternatively be used. Further, in Silver a lubricant, from the group consisting of calcium stearate or magnesium stearate may be added. However, a lubricant is not required. Calcium need not be present in Silver although it represents as the largest active ingredient in the present application. Further, no therapeutic use of calcium is even hinted at in Silver.

Other significant differences are found between Silver and the present application. Unlike Silver, the present invention includes liquid paraffin or silicone oil. Unlike Silver, the present application does not require any antioxidant. Unlike Silver, there are required binders of propylene glycol or polyethylene glycol, liquid paraffin or silicone oil. There is nothing of record which would suggest the addition of these binders. In short, Silver does not disclose a pharmaceutical formulation of calcium and Vitamin D in the specific ratio claimed (high quantity of calcium, low quantity of Vitamin D) with specific binders, nor could the same be anticipated.

At page 6 of the Office Action, Claims 1-8 and 13-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over FR-A-2 724 844 (hereinafter FR '844).

Reconsideration is requested.

As stated by the Examiner, "FR '844 does not teach all of the specific additives claimed by the applicant. Additionally, the reference does not disclose the amounts of Vitamin D and calcium salt in the same manner claimed by the applicant."

The binding agents of the present invention, propylene glycol, polyethylene glycol, liquid paraffin or silicone oil are not disclosed in FR '844. More particularly, with respect to FR '844, the formulation contains 500 mg of calcium (see page 10, line 5) unlike the present invention with 1-2 g of elemental calcium. Further, only the carbonate, pidolate, and lactate calcium salts are disclosed, and only calcium carbonate is claimed (see claim 12). Conversely, in the present invention, calcium phosphate is preferred. Its insolubility necessitates use of the specific binding agents. Since the

calcium phosphate salt is not used in FR '844, there is no need to look for the specific binding agents of the present invention. The distinction between the different salts and amount of calcium present and the binders used is a very significant one, and is the basic reason the FR' 844 patent does not render the claims of the present application patentably obvious.

Claim 1 of FR '844 specifically requires the use of a dry and wet binder, the process comprising the formation of solutions and suspensions. On page 6, line 31, it is reported that the wet granulation of calcium carbonate is mixed with polyvinyl pyrrolidone (a solid) to obtain a humid mass which is dried on an air bed (see page 7, lines 8 and 9). Other solid binders (e.g. cellulose, maltodextrines, sweeteners) may be used. However, the binders of the present invention are liquids, are not suitable for the FR '844 preparation procedure, and are, therefore, not obvious from same.

Further, the present invention is distinctly different from FR '844 in that no water is utilized. Instead, the chosen liquid binders facilitate the homogenizing of the components of the formulation. Therefore, it could not be obvious using the process of FR '844 to produce the current invention as FR' 844 teaches away from the present invention.

The Applicant notes with appreciation that Claims 9-12 would be allowable if rewritten in independent form including the limitation of the base claim and any intervening claims.

Accordingly, Applicant has amended the claims as suggested by the Examiner.

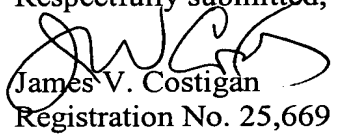
The present invention represents a significant advantage over the prior art and avoids disadvantages of the prior art compositions. The present invention is physically diverse from the prior art in that it eliminates or greatly reduces the "sand effect" of insoluble calcium salts such as calcium phosphate. Such innovation could not be predicted from the prior art which contains no teaching to suggest same.

The prior art reference cannot be easily modified to include the unique structural and functional advantages described in the present invention. The present invention results in an easily manufactured homogeneous combination of calcium and Vitamin D in a particular ratio which is palatable and encourages patient compliance. The elements of the present invention are neither disclosed nor addressed by the prior art.

It is apparent from the foregoing that it is not enough to have a combination of calcium and Vitamin D in a pharmaceutical formulation. It is the unique ratio of calcium and Vitamin D together with propylene glycol, polyethylene glycol, liquid paraffin or silicone oil binders which result in significant advantages over the prior art. The present invention provides a homogeneous distribution low dosages of Vitamin D with high dosages of calcium which is stable, bioavailable, and suitable for high-speed production machines and palatable. Additionally, the present formulation overcomes problems due to "granulation" of the calcium salt. The glycol diffuses over the calcium granules, resulting in a binding effect over the small granules of coated Vitamin D_3, resulting in a mixture having flow characteristics conducive to processing by high output machines and actually facilitates subsequent reconstitution of a dispersion. It is urged that the unique structural and functional composition of the present application is unobvious. Given the aforementioned distinctions, it is maintained that the prior art references do not teach or suggest the present invention.

For the foregoing reasons and in view of the amendments, the present claims are believed to be patentable over the references of record and to be in a condition for allowance. Such action is earnestly and respectfully solicited.

Respectfully submitted,



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Version with Markings to Show Changes Made:

1. (Amended) A [P]pharmaceutical composition containing as active principles Vitamin D [associated to] and a calcium salt [characterized in that it] which comprises a binding agent [chosen in] selected from the group consisting of[:] propylene glycol, a polyethylene glycol [presenting a] of molecular weight [comprised] between 300 and 1500, liquid paraffin [or] and silicone oil, [and that the] said Vitamin D [is] being present [at the rate of] in an amount of 500-1000 I.U. of Vitamin D and said calcium salt being present in a ratio of 1- 2 g of calcium , calculated as elemental calcium, for each 500-1000 I.U. of Vitamin D.

2. (Amended) A [P]pharmaceutical composition according to Claim 1, in which the calcium used is in the form of a salt [chosen in] selected from the group consisting of[:] phosphate, glycerophosphate, carbonate, bicarbonate, lactate, citrate, tartrate, gluconate[,] and chloride.

7. (Amended) A [P]pharmaceutical composition [(bag)] in a sachet dosage form according to Claim 1, containing the propylene glycol in a quantity comprised between 5-15% by weight calculated on the total composition.

8. (Amended) A [P]pharmaceutical [composition (] tablet [)] according to Claim 1, containing liquid paraffin or silicone oil.

9. (Amended) A [P]pharmaceutical composition in a sachet dosage form [according to Claim 7,] characterized as follows:

Tribasic calcium phosphate	3.100 g
(corresponding to 1200 mg of Ca^{++})	
Cholecalciferol (Vit. D_3) 100,000 IU/g	0.008 g
(corresponding to 800 IU)	
Propylene glycol	0.800 g
[E110] Sunset Yellow	0.002 g

Colloidal silica	0.120 g
Lemon flavo[u]ring	0.100 g
Microcrystalline cellulose- MCC	0.200 g
Sodium saccharin	0.015 g
Anhydrous citric acid	0.165 g
Sucrose monopalmitate	0.120 g
Mannitol q.s. to	7.000 g

10. (Amended) A [P]pharmaceutical composition [according to Claim 7,] in a sachet dosage form characterized as follows:

Tribasic calcium phosphate	3.100 g
(corresponding to 1200 mg of Ca^{++})	
Cholecalciferol (Vit. D_3) 100,000 IU/g	0.008 g
(corresponding to 800 IU)	
Polyethylene glycol	0.800 g
[E110] Sunset Yellow	0.002 g
Colloidal silica	0.120 g
Lemon flavo[u]ring	0.100 g
Microcrystalline cellulose- MCC	0.200 g
Sodium saccharin	0.015 g
Anhydrous citric acid	0.165 g
Sucrose monopalmitate	0.120 g
Mannitol q.s. to	7.000 g

11. (Amended) A [P]pharmaceutical composition [according to Claim 8,] in a tablet dosage form characterized as follows:

Tribasic calcium phosphate	3.100 g
(corresponding to 1200 mg of Ca^{++})	
Cholecalciferol (Vit. D_3) 100,000 IU/g	0.008 g
(corresponding to 800 IU)	
Liquid paraffin	0.500 g
Sodium carboxymethyl cellulose	0.050 g
Sodium saccharin	0.015 g
Orange flavo[u]ring	0.100 g
Sorbitol q.s. to	4.400 g

12. (Amended) A [P]pharmaceutical composition [according to Claim 8,] in a tablet dosage form characterized as follows:

Tribasic calcium phosphate	3.100 g
(corresponding to 1200 mg of Ca^{++})	
Cholecalciferol (Vit. D_3) 100,000 IU/g	0.008 g
(corresponding to 800 IU)	
Silicone oil	0.500 g
Sodium carboxymethyl cellulose	0.050 g
Sodium saccharin	0.015 g
Orange flavo[u]ring	0.100 g
Sorbitol q.s. to	4.400 g

13. (Amended twice) A [P]process for the preparation of a pharmaceutical composition according to Claim 1, characterized by the following steps:
a) In a granulator turning at high speed, distributing [the] a binding agent, consisting of propylene glycol or low molecular-weight polyethylene glycols over [the] a calcium salt;
b) Adding [the] colloidal silica, approximately 25% of [the] mannite, [the] citric acid, and [the] sodium saccharin, and mixing for [the time required] an appropriate time and at [the] an appropriate speed to produce a first mixture;
c) Adding a second mixture, prepared separately, consisting of sucrose palmitate, a suspending agent, flavoring, a colo[u]ring agent, [the remaining part] approximately 75% of the mannite and the Vitamin D_3, and mixing together with the [rest of the preparation] first mixture to form a granulate; and
d) Distributing the granulate thus obtained into [bags] sachets .

14. (Amended twice) A [P]process for the preparation of a pharmaceutical composition according to Claim 1, characterized by the following steps:
a) In a granulator turning at high speed, placing [the] a binding agent, consisting of liquid paraffin or silicon oil, over [the] a calcium salt;
b) Adding in order, to a mixture of colloidal silica, carboxymethyl cellulose and sodium saccharin previously sifted, the Vitamin D_3 and [the] sorbitol, mixing thoroughly every time before a new ingredient is added, and pouring the mixture into the rotating granulator and mixing for [the required] an appropriate time and at [the] an appropriate speed to form a granulate; and
c) Compressing the granulate to [the] a required weight to obtain [the desired] tablets.